

# Diagnosis & Treatment of *Clostridium difficile* Infection (CDI)

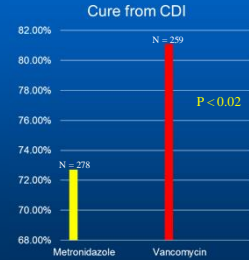
**Herbert L. DuPont, MD, MACP**

Director, Center for Infectious Diseases, University of Texas School of Public Health  
Mary W. Kelsey Distinguished Chair in Medical Sciences, University of Texas Medical School, Houston  
President, Kelsey Research Foundation

Additional appointments as Professor: University of Texas and Baylor Graduate Schools of Biomedical Science, MD Anderson Cancer Center, University of Houston

## Vancomycin Versus Metronidazole

- In a double-blind randomized trial vancomycin was superior to metronidazole for all cases from mild to severe



Johnson S, et al. Clin Infect Dis 2014;59:345-54

## First Step: Make Diagnosis

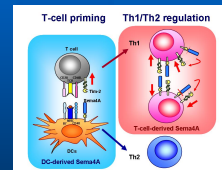
**Make an Early Diagnosis of CDI. Consider Stopping Current Antibiotics and Start CDI Treatment**



Making the diagnosis: diarrhea plus positive fecal test for *C. difficile* toxin(s):

- EIA lacks sensitivity;
- Toxigenic culture and Tissue culture cytotoxicity assay takes 3 days
- PCR overly sensitive and picks up carriage
- Two step methods have been developed (e.g. glutamate dehydrogenase + EIA or PCR)
- Fecal CD toxin test plus finding inflammatory markers in stool suggests; Finding pseudomembranous colitis by endoscopy confirms the diagnosis

## Immune Response in *C. difficile* Infection and Diarrhea



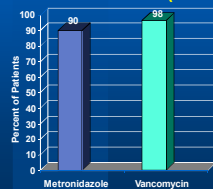
- Antitoxin A IgG antibody rises most common in subclinical infection; both subclinical infection and serum antibodies are protective against *C. difficile* diarrhea
- Development of a serum antitoxin A IgG or IgM antibody response predicts those who will not relapse

Kyne L, et al. N Engl J Med 2000;342:390-7  
Kyne L, et al. Lancet 2001;357:189-93

## Oral Vancomycin vs Metronidazole in Mild and Severe CDI

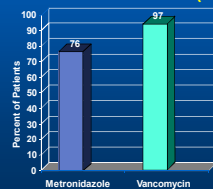
- 172 patients enrolled and 150 completed the trial

**Clinical Cure in Mild Disease (n=81)**



P = NS

**Clinical Cure in Severe Disease (n=69)**

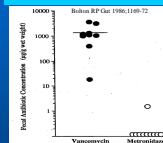


P = 0.02

Zar FA, et al. Clin Infect Dis. 2007;45:302-307.

## Relative Cost of Various CDI Treatments

**Pharmacokinetic Data with Metronidazole**



Vancomycin (Oral)



Fidaxomicin

**Average Wholesale Prices For 10 Days**

~ Metronidazole 500 mg PO TID \$25.00

~ Vancomycin 125 mg PO QID Capsules \$1,300 Oral liquid <\$200

~ Fidaxomicin 200 mg PO BID \$2,500

Is 10% ↓ in recurrence with fidaxomicin worth additional cost? If you factor in prevention of recurrence it may be! Before prescribing fidaxomicin be sure insurance plan will allow continuance of drug as an outpatient

## Treatment Strategies for Recurrent CDI



Vancomycin (Oral)

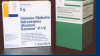
Fidaxomicin



*Saccharomyces boulardii* (Florastor)



Rifaximin (Xifaxan)



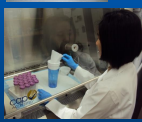
IVIG

- 1<sup>st</sup> recurrence - initial therapy can be repeated (not metronidazole)
- Oral vancomycin
  - Tapered dose (125 mg 4 times a day down to 125 mg once every three days over 6 weeks)
  - Pulse dose (125 mg or 500 mg every 3 days for 3 weeks)
  - *Saccharomyces boulardii* 500 mg bid x 14 days after oral vancomycin
- Fidaxomicin 200 mg twice a day for 10-20 days
- Rifaximin 550 mg twice a day for 4 weeks alone or followed by 2 weeks of *S. boulardii* (above dose)
- Fecal microbiota transplant (FMT) most effective treatment for ≥ 3 bouts of CDI

DuPont HL. Diagnosis and management of *Clostridium difficile* infection. Clinical Gastro Hepatol. 2013;11:1216-23

## For Depletion of Diversity of Microflora - Fecal Microbiota Transplantation (FMT)

- ~ 50 g of stool is collected from healthy donor
- CDI patients are randomized to receive fresh, frozen or lyophilized fecal bacteria
- 120 patients treated so far in two studies with >90% cure rates
- We have moved to enteric coated capsules & enemas for administration



## *C. difficile* Diarrhea (CDI) Directions of Future Research

### To Determine:

- Optimal methods to diagnose CDI that differentiates between disease & colonization
- Treatment of primary and recurrent CDI (for cure without future recurrence)
- Development of novel therapeutic drugs and biologic agents (advanced probiotics)
- Prevention of CDI in high risk people



*C. difficile* Research Team at Baylor St. Luke's